3/10/2003

Uploading taxol.str

L3 STRUCTURE UPLOADED

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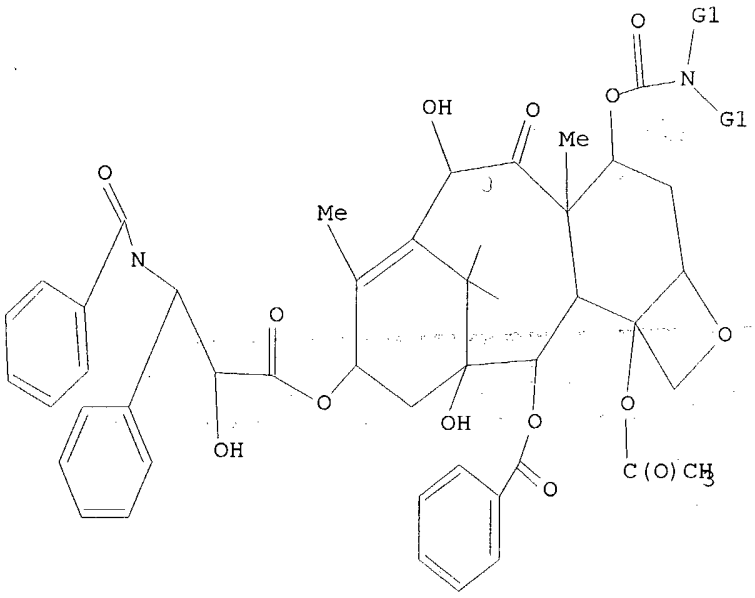
L3 HAS NO ANSWERS
L3 STR



G1 Cb,Cy,Hy,Ak,Me,Et,n-Pr,i-Pr,n-Bu,i-Bu,t-Bu,Ph,H

Structure attributes must be viewed using STN Express query preparation.

=> s l3 sss full

FULL SEARCH INITIATED 17:20:42 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 210 TO ITERATE

100.0% PROCESSED 210 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L4 0 SEA SSS FUL L3

=>
Uploading taxol.str

L1 STRUCTURE UPLOADED

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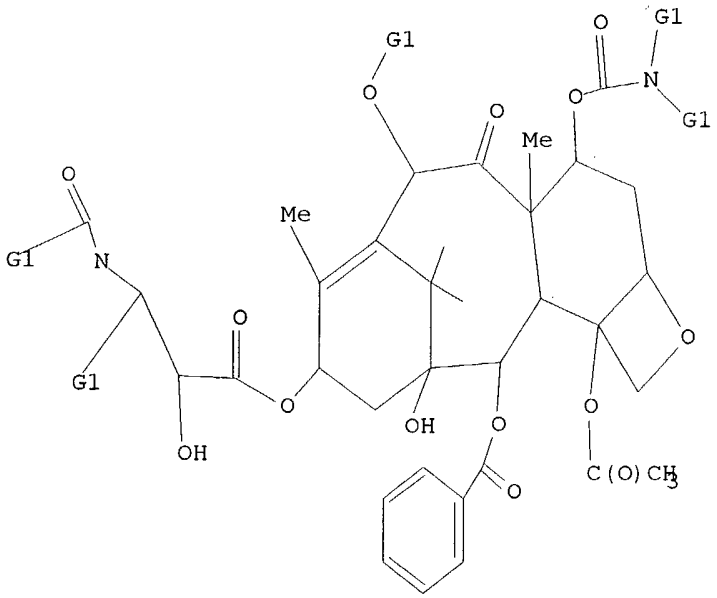
L1 HAS NO ANSWERS
L1 STR



G1 Cb,Cy,Hy,Ak,Me,Et,n-Pr,i-Pr,n-Bu,i-Bu,t-Bu,Ph,H

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss full

FULL SEARCH INITIATED 17:25:55 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 248 TO ITERATE

100.0% PROCESSED 248 ITERATIONS 27 ANSWERS

> s l2

L3 12 L2

> d l3 1-12 ibib abs hitstr

L3 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:640738 CAPLUS
DOCUMENT NUMBER: 131:267037
TITLE: Water soluble paclitaxel derivatives for treatment of tumors
INVENTOR(S): Li, Chun; Wallace, Sidney; Yu, Dong-fang; Yang, David
PATENT ASSIGNEE(S): Pg-Txl Company, L.P., USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9949901	A1	19991007	WO 1999-US6870	19990330
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9934556	A1	19991018	AU 1999-34556	19990330
EP 1028756	A1	20000823	EP 1999-916188	19990330
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1998-50662 A2 19980330
WO 1999-US6870 W 19990330

AB Disclosed are water sol. compns. of paclitaxel and docetaxel formed by conjugating the paclitaxel or docetaxel to a water sol. polymer such as poly-glutamic acid, poly-aspartic acid or poly-lysine. Also disclosed are methods of using the compns. for treatment of tumors, auto-immune disorders such as rheumatoid arthritis. Other embodiments include the coating of implantable stents for prevention of restenosis. Glutamic acid-paclitaxel copolymer (I) was prepd. by the reaction of polyglutamic acid with paclitaxel. Water sol. I had antitumor activity against mammary carcinoma and mammary ovarian carcinoma and was more effective than paclitaxel on equiv. mg paclitaxel basis.

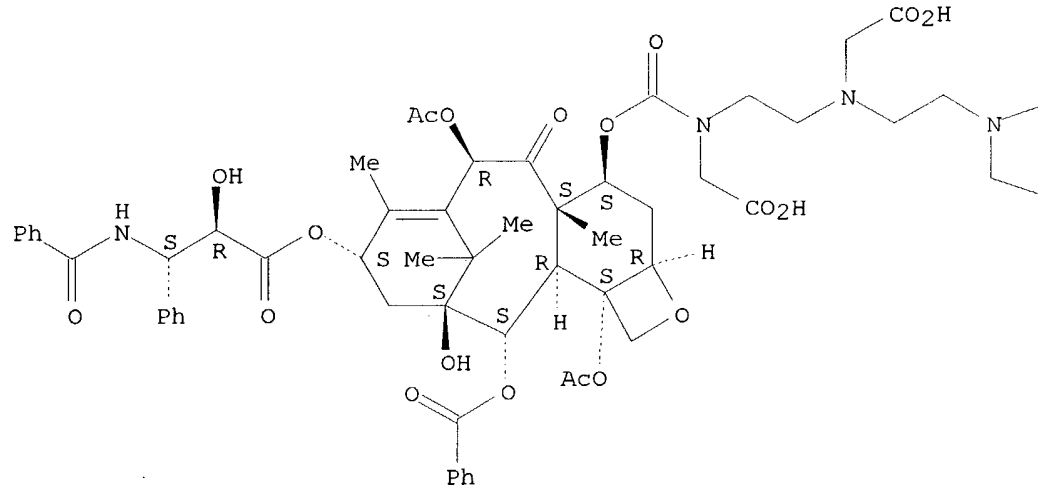
IT **245322-09-2P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(water sol. paclitaxel derivs. for treatment of tumors)

RN 245322-09-2 CAPLUS
CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-

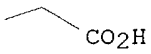
4-[[[[2-[[2-[bis(carb[redacted]methyl)amino]ethyl](carboxymet[redacted])amino]ethyl](car
boxymethyl)amino]carbonyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-
dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-
cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (.alpha.R,.beta.S)- (9CI) (CA
INDEX NAME)

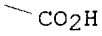
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B





REFERENCE COUNT: 4
REFERENCE(S):
(1) Brem; US 5626862 A 1997 CAPLUS
(2) Butterfield; US 5730968 A 1998 CAPLUS
(3) Li, C; Pharmaceutical Research 1996, V13(9), PS-368
(4) Mongelli; US 5473055 A 1995 CAPLUS

L3 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:282391 CAPLUS
DOCUMENT NUMBER: 130:352485
TITLE: Synthetic studies of sialo-glycoconjugates
AUTHOR(S): Takahashi, T.; Tsukamoto, H.; Kurosaki, M.; Yamada, H.
CORPORATE SOURCE: Department of Chemical Engineering, Tokyo Institute of Technology, Tokyo, Japan
SOURCE: Tennen Yuki Kagobutsu Toronkai Koen Yoshishu (1997), 39th, 49-54
CODEN: TYKYDS
PUBLISHER: Nippon Kagakkai

DOCUMENT TYPE: Journal
LANGUAGE: Japanese
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB N-Acetyl neuraminic acid (Neu5Ac) is incorporated at the nonreducing terminal position of glycoconjugates which are found in cell membranes and in nervous systems of various living organisms. These sialyl conjugates play an essential role in biol. mol. recognition processes, such as cell adhesion and differentiation phenomena. For the elucidation of these biol. properties and functions, the supply of natural and nonnatural sialyl conjugates with a definite structures is indispensable. The ulosonic acids such as Neu5Ac, KDO, and KDN have the .alpha.-ketoacid moieties which exist in a 6-membered cyclic hemiacetal form. To establish a general synthetic method for monosaccharides contg. the .alpha.-ketoacid structures, we examd. the synthesis of Neu5Ac utilizing alkylation of 2-alkoxy-2-cyanoacetate [I; R= Me3CSiMe2 (TBS)], an acylanion equiv. of alkyl glyoxylate, with bromide (II; R = Br; MOM = CH2OMe) derived from the com. available D-glycero-D-gulo-heptose-1,4-lactone, to give II [R = C(CN)(OTBS)CO2CMe3]. We also examd. the syntheses of KDO and KDN based on alkylation of 2-alkoxy-2-cyanoacetate [I; R = 1-ethoxyethyl (EE)] with the sugar-derived iodide (III; R = iodo) and triflate (IV; R = CF3SO3) to give III [R = C(CN)(OEE)CO2CMe3] and IV [R = C(CN)(OEE)CO2CMe3], resp. One of the most difficult problem in the synthesis of sialyl conjugate is the stereoselective glycosidation of sialic acid with .alpha.-glycosidic linkage. First, we examd. a new method for .alpha.-glycoside formation of sialyl conjugate utilizing the concept of "long-range participation". When 2-methylthioethyl ester was introduced into the carboxylic acid in the sialic acid as neighboring group (V) and DME was used as solvent, highly .alpha.-selective glycosylation was achieved in moderate yields. To improve the yields, we examd. alkylation of 2-alkoxy-2-phenylthioacetate (VI; R = H) 34 with allyl bromide (Q-Br) 36 to form an intermediate (VI; R = Q) followed by an intamol. glycosylation to an intermediate (VII). Phenylthio-group serves as not only a stabilizer of an enolate in the alkylation but also a leaving group in the glycosylation. This method are underway in our lab.

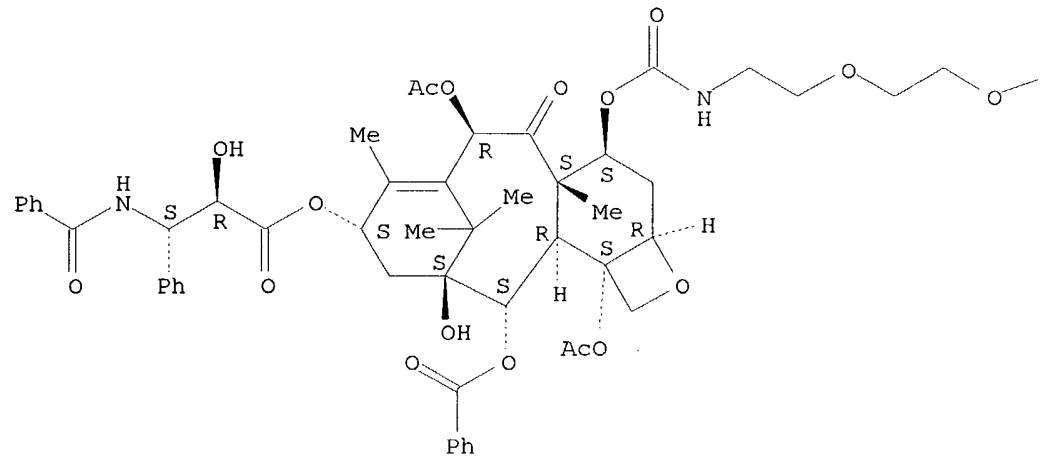
IT **202194-43-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of N-acetylneuraminic acid, KDN, KDO, and sialo-glycoconjugates via alkylation of alkoxycyanoacetate with pentahydroxyheptenyl bromide and hexahydroxyheptyl triflate)

RN 202194-43-2 CAPLUS

CN .alpha.-Neuraminic acid, N-acetyl-2-O-[2-[2-[2-[[[[(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-9-[(2R,3S)-3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]amino]ethoxy]ethoxy]ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemis[redacted].

PAGE 1-A



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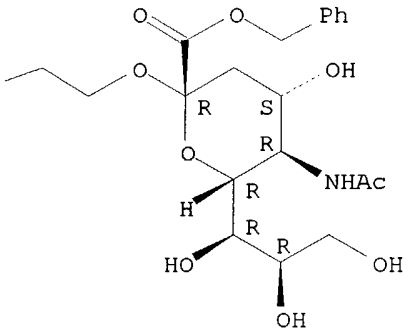
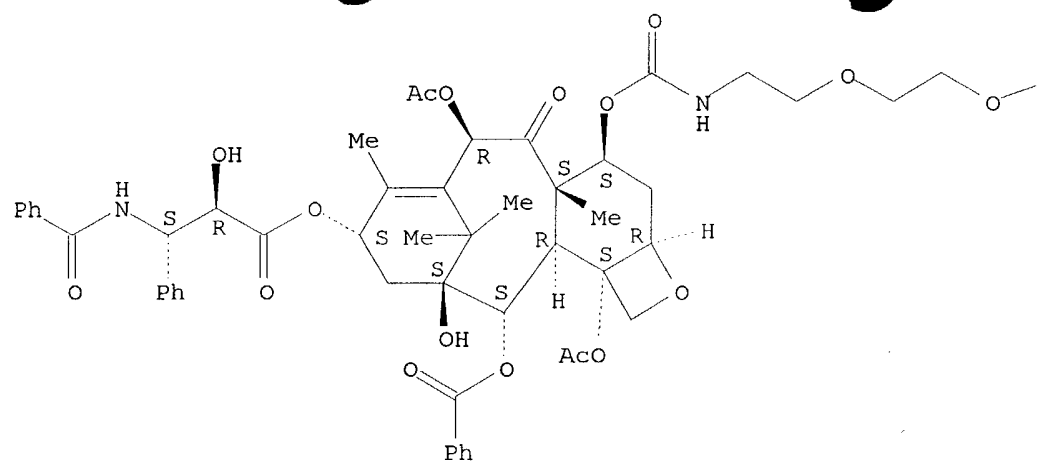


IT **225235-44-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of N-acetylneuraminic acid, KDN, KDO, and sialo-glycoconjugates
via alkylation of alkoxycyanoacetate with pentahydroxyheptenyl bromide and hexahydroxyheptyl triflate)
RN 225235-44-9 CAPLUS
CN .alpha.-Neuraminic acid, N-acetyl-2-O-[2-[2-[2-

[[[[(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-9-[(2R,3S)-3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]amino]ethoxy]ethoxy]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



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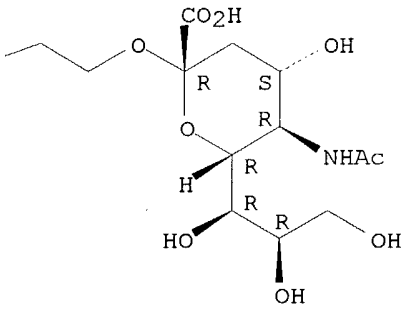


L3 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:64977 CAPLUS
DOCUMENT NUMBER: 130:119580
TITLE: Identification of molecular targets of drugs or toxins
INVENTOR(S): Makowski, Lee; Makowski, Diane R.; Sanganee, Hitesh J.
PATENT ASSIGNEE(S): Florida State University, USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902733	A1	19990121	WO 1998-US14082	19980707
W: CN, JP, KR				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 990051	A1	20000405	EP 1998-945752	19980707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-51780 19970707
US 1997-51781 19970707

AB Identification of the mol. targets of a drug or toxin is the first step in understanding how the drug or toxin works, and important advance in learning how to improve a drug or assess the risks due to a toxin. The primary action of a drug usually involves binding to a protein; secondary actions may express themselves in the form of side effects and in some cases may be due to binding to other proteins. Consequently, it is useful to identify all physiol. relevant sites of action of a drug or toxin. A simple method for obtaining a list of the potential targets of a drug, toxin or other biol. active substance (referred to collectively as ligands) involves a multistep process. The first step is screening a protein or peptide library to identify library members that exhibit high affinity for a particular ligand. The second step involves searching of sequence data bases for proteins that contain the sequences of the library members shown to have high affinity for the ligand. The proteins thus identified constitute a list of potential targets for the ligand. If random peptide libraries have been used, the position of identified consensus sequences within the identified protein constitutes an identification of the potential ligand binding site on the target.

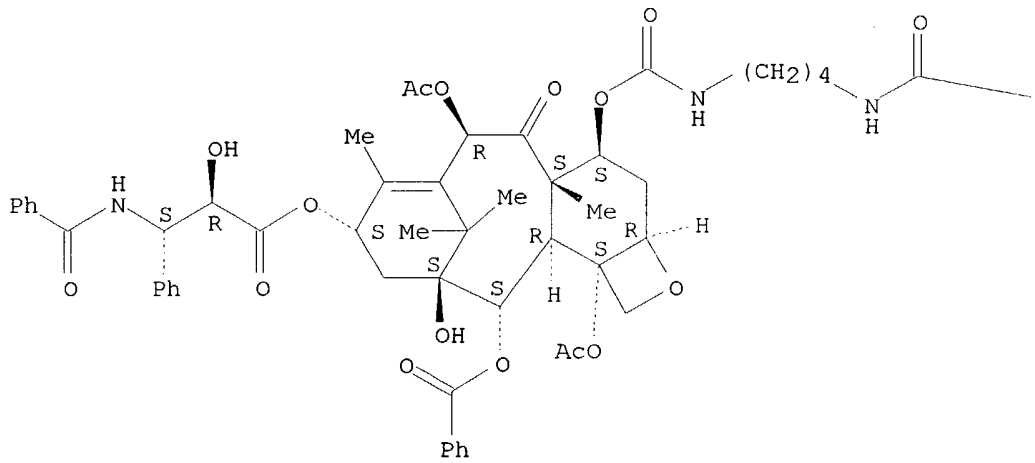
IT **219950-34-2P 219950-36-4P 219950-38-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(drug or toxin mol. target identification)

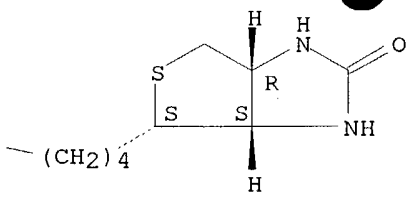
RN 219950-34-2 CAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-4-[[[[4-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]butyl]amino]carbonyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





PAGE 1-B

RN 219950-36-4 CAPLUS
CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,

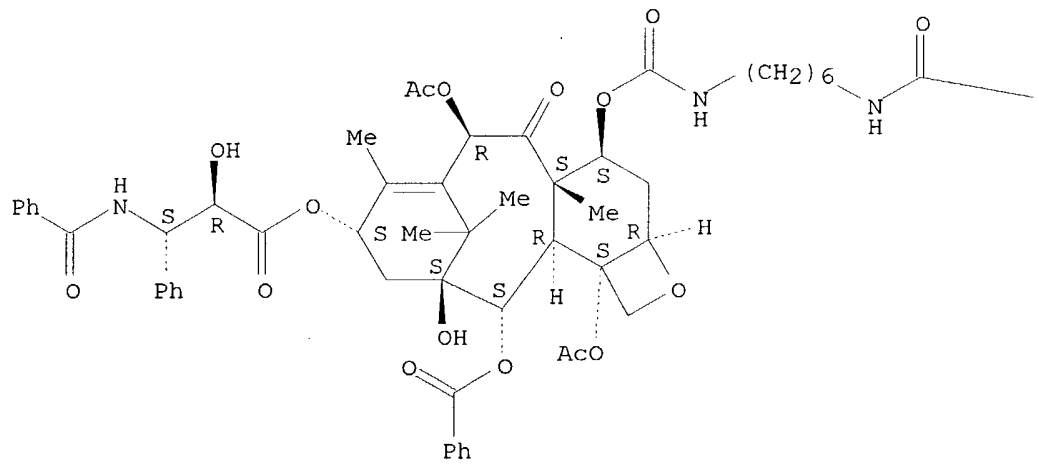
(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-

4-[[[[6-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-

oxopentyl]amino]hexyl]amino]carbonyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-
dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-
cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (.alpha.R,.beta.S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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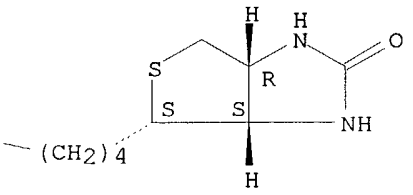


RN 219950-38-6 CAPLUS
CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,

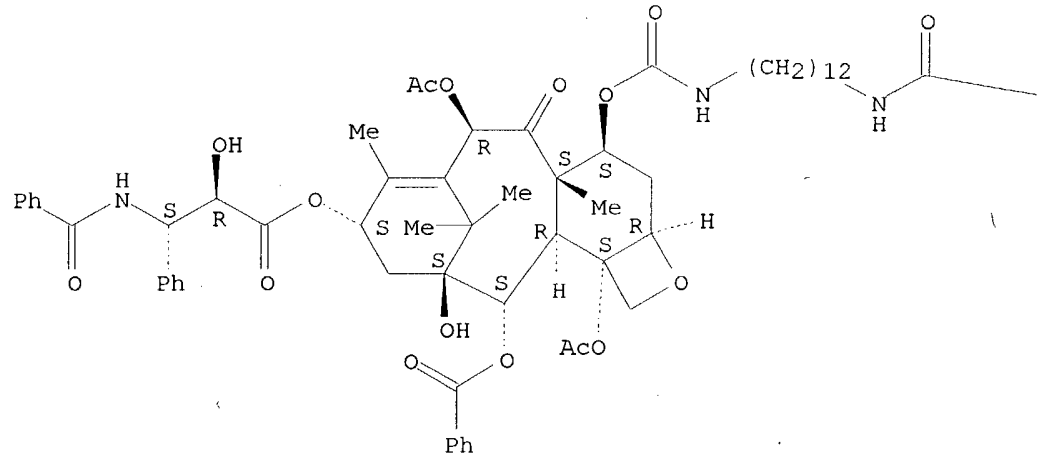
(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-

4-[[[[12-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-

1-oxopentyl]amin[redacted]odecyl]amino]carbonyl]oxy]-
2a,3,4,4a,5,6,9,[redacted]11,12,12a,12b-dodecahydro-11-h[redacted]oxy-4a,8,13,13-
tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl
ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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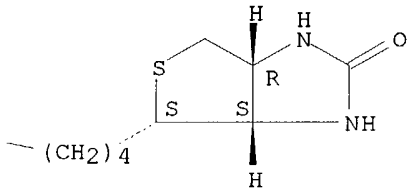


REFERENCE COUNT: 6
REFERENCE(S):
(1) Bruno, J; Biochemical and Biophysical Research Communications 1997, V236, P344 CAPLUS
(2) Cwirla, S; Peptides on phage: a vast library of peptides for identifying ligands 1990, V87, P6378 CAPLUS
(3) Devlin, J; Random Peptide Libraries: A source of specific protein binding molecules 1990, V249, P404 CAPLUS
(4) Dower; US 5432018 A 1995 CAPLUS
(5) McCoy; US 5635182 A 1997 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:48806 CAPLUS
DOCUMENT NUMBER: 128:140940
TITLE: Design and synthesis of a water-soluble taxol analog: taxol-sialyl conjugate
AUTHOR(S): Takahashi, Takashi; Tsukamoto, Hirokazu; Yamada, Haruo
CORPORATE SOURCE: Department of Chemical Engineering, Tokyo Institute of
Technology, Tokyo, 152, Japan

SOURCE: [redacted] Bioorg. Med. Chem. Lett. (1998), 8(1), 113-116
CODEN: BMCLE8; ISSN: 0960-894[redacted]
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Glycosidation, using the methylthio deriv. of N-acetylneuraminic acid, of a linker alc. in DME with "long-range participation" produced the .alpha.-glycosyl linkage with high stereoselectivity. The .alpha.-linked sialic acid was introduced in taxol without protection of the alc. functionality in sialic acid. The taxol-sialyl conjugate was tested for water soly., microtubule binding and cytotoxicity assay.

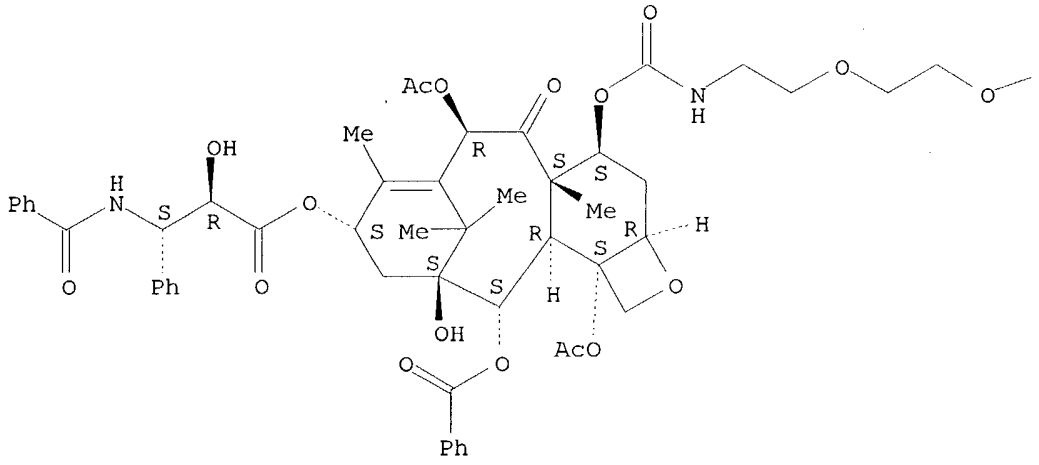
IT **202194-38-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(design and prepn. of a water-sol. taxol analog)

RN 202194-38-5 CAPLUS

CN .alpha.-Neuraminic acid, N-acetyl-2-O-[2-[2-[2-[[[[(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-9-[(2R,3S)-3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]amino]ethoxy]ethoxy]ethyl]-, monosodium salt (9CI) (CA INDEX NAME)

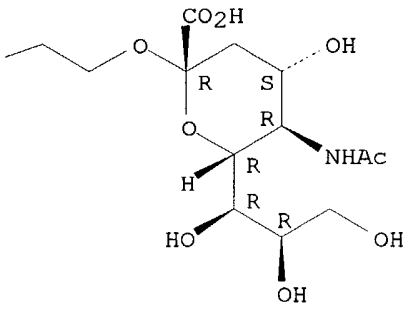
Absolute stereochemistry. Rotation (-).

PAGE 1-A



● Na

PAGE 1-B

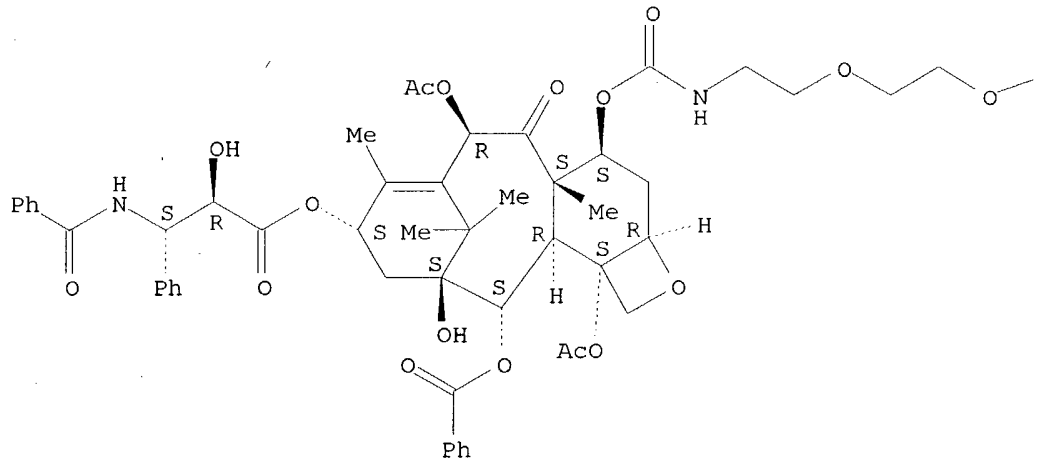


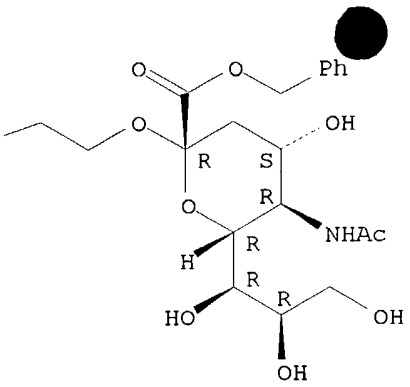
IT **202194-43-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(design and prepn. of a water-sol. taxol analog)
RN 202194-43-2 CAPLUS
CN .alpha.-Neuraminic acid, N-acetyl-2-O-[2-[2-[2-

[[[[(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-9-[(2R,3S)-3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]amino]ethoxy]ethoxy]ethyl]-, phenylmethyl ester (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





L3 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:231372 CAPLUS
DOCUMENT NUMBER: 126:308799
TITLE: High-molecular-weight polymer-based prodrugs
INVENTOR(S): Greenwald, Richard B.; Pendri, Annapurna
PATENT ASSIGNEE(S): Enzon, Inc., USA
SOURCE: U.S., 11 pp. Cont. of U.S. Ser. No. 140,346, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5614549	A	19970325	US 1995-380873	19950130
US 5880131	A	19990309	US 1995-537207	19950929
CA 2208841	AA	19960808	CA 1996-2208841	19960130
WO 9623794	A1	19960808	WO 1996-US1459	19960130
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN				
AU 9649133	A1	19960821	AU 1996-49133	19960130
AU 705147	B2	19990513		
EP 807115	A1	19971119	EP 1996-905345	19960130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
JP 10513187	T2	19981215	JP 1996-523755	19960130
US 5840900	A	19981124	US 1996-700269	19960820
US 5965566	A	19991012	US 1997-914927	19970820
US 6127355	A	20001003	US 1999-277230	19990326

PRIORITY APPLN. INFO.:
US 1992-934131 B2 19920821
US 1993-28743 B2 19930309
US 1993-140346 B2 19931020
US 1995-380873 A2 19950130
US 1995-537207 A 19950929
WO 1996-US1459 W 19960130
US 1996-700269 A2 19960820
US 1997-914927 A1 19970820

OTHER SOURCE(S): MARPAT 126:308799

AB Water-sol. prodrugs comprise hydrolyzable linkages between a polymer portion and a biol. active nucleophile, preferably taxoids. PEG 40,000 dicarboxylic acid bis(taxol-2'-diester) was prepd. and injected to P388/0 murine lymphoid neoplasm-infected mice to det. the ability of the prodrug

to increase the life span of the mice.

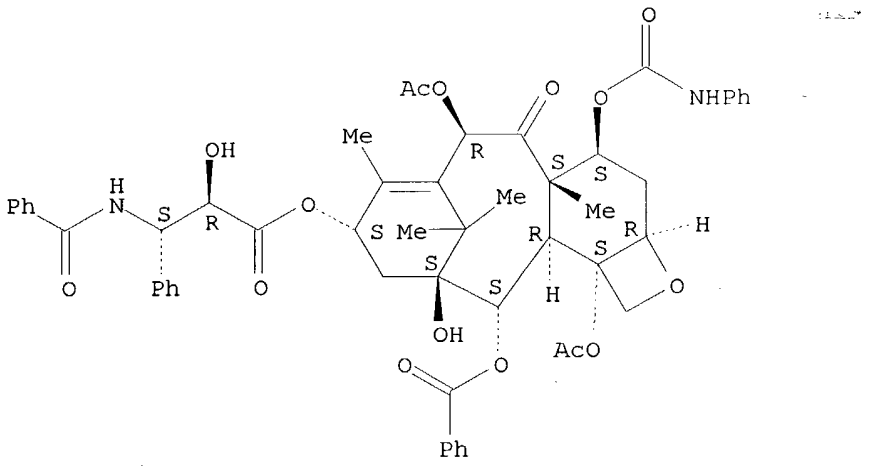
IT **161742-57-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of high-mol.-wt. polymer-based water-sol. prodrugs)

RN 161742-57-0 CAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-

[[(phenylamino)carbonyl]oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester,
[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:148858 CAPLUS
DOCUMENT NUMBER: 126:162276
TITLE: Androgenic receptor-binding phenylthiohydantoins for diagnosis and treatment of prostate cancer
INVENTOR(S): Sovak, Milos; Bressi, Jerome C.; Douglass, James Gordon, III; Campion, Brian; Wrasidlo, Wolfgang
PATENT ASSIGNEE(S): Biophysica Foundation, USA; Sovak, Milos; Bressi, Jerome C.; Douglass, James Gordon, III; Campion, Brian; Wrasidlo, Wolfgang
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

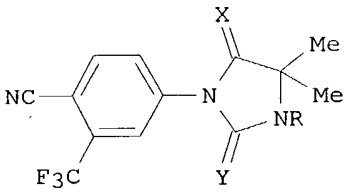
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9700071	A1	19970103	WO 1996-US10286	19960613
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
US 5656651	A	19970812	US 1995-491130	19950616
CA 2225484	AA	19970103	CA 1996-2225484	19960613

AU 9663329	A1	19970115	AU 1996-63329	19960613
AU 712609	B2	19991111		
EP 854716	A1	19980729	EP 1996-922463	19960613
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 10510845	T2	19981020	JP 1996-503330	19960613

PRIORITY APPLN. INFO.: US 1995-491130 19950616
WO 1996-US10286 19960613

OTHER SOURCE(S): MARPAT 126:162276

GI



I

AB Substituted phenylthiohydantoins (I; X, Y = O, S, NH; R = aliph., aryl, or aralkyl linking group) are provided for use in detecting tumor cells having androgenic receptors. These compds. can be used for specific targeting to the androgenic receptor-contg. cells of cytostatic and/or cytotoxic agents, heavy or light radioactive or radiopaque atoms, etc. for detection and treatment of cancer cells contg. androgenic receptors (e.g. prostate cancer cells). Thus, cycloaddn. of 2-[[[N-(tert-butoxycarbonyl)amino]ethyl]amino]-2-cyanopropane to 2-trifluoromethyl-4-isothiocyanatobenzonitrile produced I (X = NH, Y = S, R = CH2CH2NHCO2Bu-t) (BP-136), which was converted to the unprotected aminoethyl deriv. (BP-138) with HCl. BP-138 was conjugated with 2'-(triethylsilyloxy)-7-(p-nitrophenoxycarbonyl)paclitaxel (prepn. given) to produce a targeted cytotoxic agent.

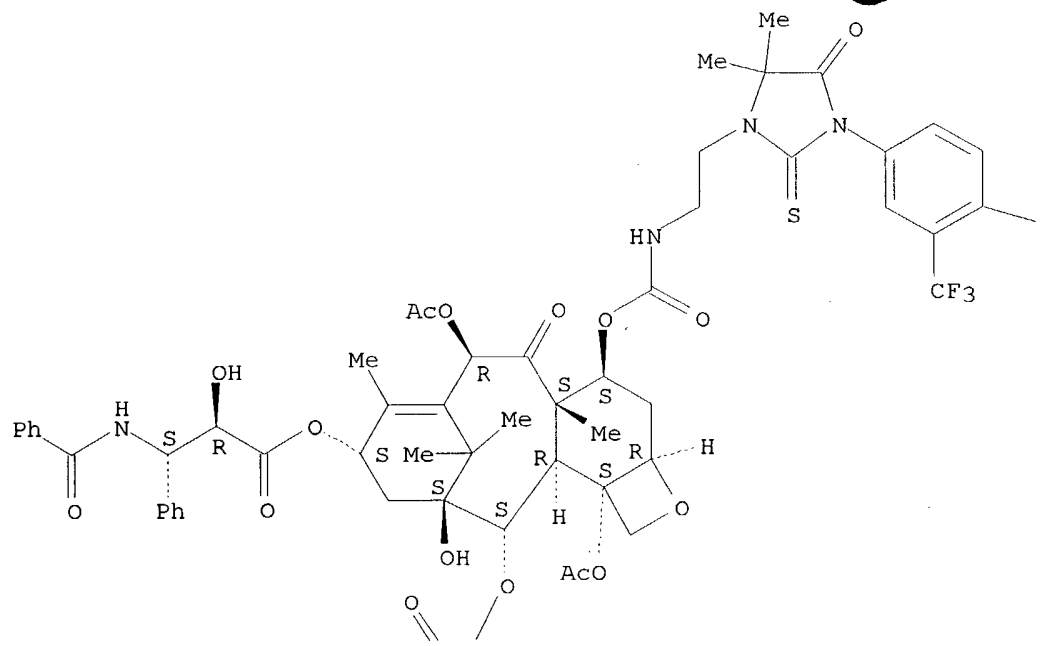
IT **186040-53-9P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(androgenic receptor-binding phenylthiohydantoins for diagnosis and treatment of prostate cancer)

RN 186040-53-9 CAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-4-[[[[2-[3-[4-cyano-3-(trifluoromethyl)phenyl]-5,5-dimethyl-4-oxo-2-thioxo-1-imidazolidinyl]ethyl]amino]carbonyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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CN

PAGE 2-A

L3 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:	1997:105187 CAPLUS
DOCUMENT NUMBER:	126:113164
TITLE:	Novel taxoids as antiproliferative agents
INVENTOR(S):	Sovak, Milos; Douglass, James G.; Bressi, Jerome C.; Seligson, Allen
PATENT ASSIGNEE(S):	Biophysica Foundation, USA; Sovak, Milos; Douglass, James G.; Bressi, Jerome C.; Seligson, Allen
SOURCE:	PCT Int. Appl., 55 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9638138	A1	19961205	WO 1996-US8245	19960531
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
US 5801191	A	19980901	US 1995-457674	19950601
CA 2222299	AA	19961205	CA 1996-2222299	19960531
AU 9659622	A1	19961218	AU 1996-59622	19960531
AU 713097	B2	19991125		
EP 833628	A1	19980408	EP 1996-916900	19960531
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 10509461	T2	19980914	JP 1996-536740	19960531

PRIORITY APPLN. INFO.: US 1995-457674 19950601
WO 1996-US8245 19960531

OTHER SOURCE(S): MARPAT 126:113164

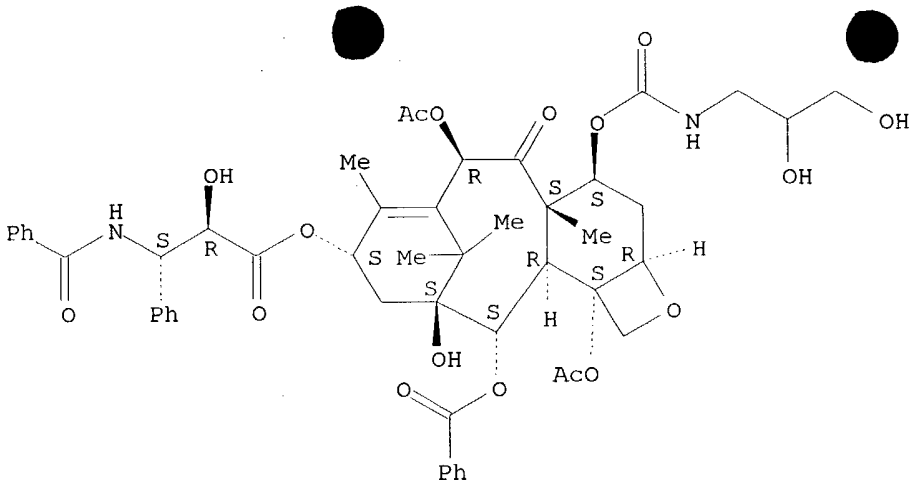
AB Novel taxoids are provided having enhanced water soly. and/or improved pharmacol. properties as compared to paclitaxel. The subject taxoids comprise a functional group attached to a paclitaxel at the C-2' and/or C-7 position by a linking group. Functional groups present in the subject taxoids may be hydrophilic chains, groups capable of in vivo conversion to hydrophilic chains, targeting moieties capable of specifically binding with cellular receptors and water sol. polymers of at least 5 kD. The subject taxoids find use in the treatment of hosts suffering from a cellular proliferative disease.

IT **186032-89-3P**, BP 187 **186040-53-9P**, BP 196
186040-55-1P, BP 184
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(novel taxoids as antiproliferative agents)

RN 186032-89-3 CAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-4-[[[(2,3-dihydroxypropyl)amino]carbonyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



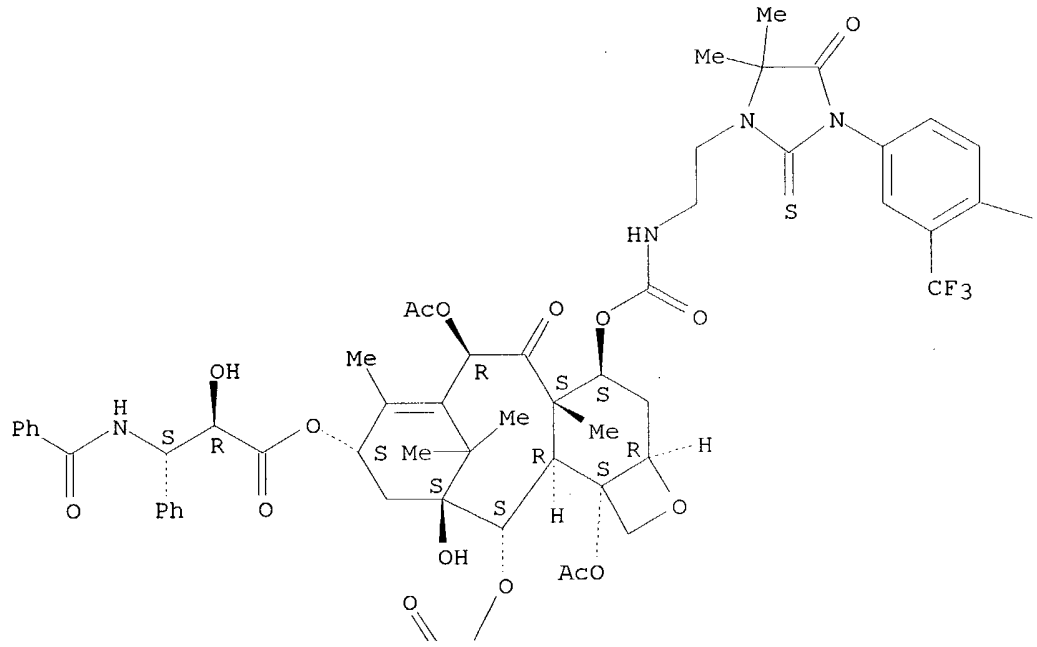
RN 186040-53-9 CAPLUS
CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-4-[[[[2-[3-[4-cyano-3-(trifluoromethyl)phenyl]-5,5-dimethyl-4-oxo-2-thioxo-1-

imidazolidinyl]ethyl]amino]carbonyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-

[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

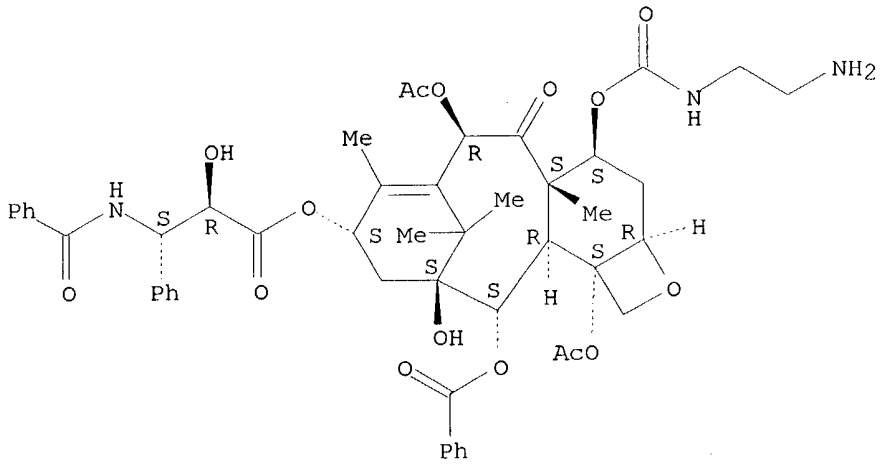
PAGE 1-A



CN

RN 186040-55-1 CAPLUS
CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, 6,12b-bis(acetyloxy)-4-[[[(2-aminoethyl)amino]carbonyl]oxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



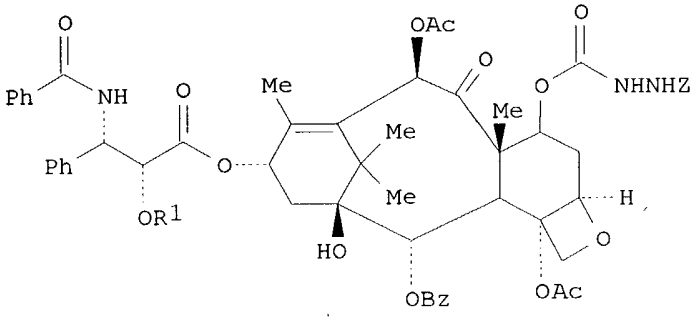
L3 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:537798 CAPLUS
DOCUMENT NUMBER: 125:196059
TITLE: Taxol-7-carbazates with improved water-solubility and/or enhanced therapeutic activity
INVENTOR(S): Greenwald, Richard B.; Pendri, Annapurna
PATENT ASSIGNEE(S): Enzon, Inc., USA
SOURCE: U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 140, 346, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUN 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5547981	A	19960820	US 1994-198194	19940217

PRIORITY APPLN. INFO.: US 1993-28743 B2 19930309
US 1993-140346 B2 19931020

OTHER SOURCE(S): CASREACT 125:196059; MARPAT 125:196059
GI



I

AB Disclosed are 7-substituted taxoid derivs., in particular taxol-7-carbazates which have improved water-soly. and/or enhanced therapeutic activity and methods of making the same. The preferred taxoid derivs. have the formula I, wherein Z is H or (C:Y)nXR, Y = O or S; X = CH2 or O; n = zero or a pos. integer, preferably one; with the proviso that when n = 0, X = CH2 ; R = C1-C4-alkyl, haloalkyl, carboxyalkyl, thioalkyl, sulfonylalkyl, Ph, hydroxyphenyl, aminophenyl, carboxyphenyl, a polyalkyleneoxide homopolymer or water sol. polyalkyleneoxide contg. copolymer, having a mol. wt. of from about 1,000 to about 20,000; R1 = H or (C:O)CH2WR2; W = O, N--L, S or SO2 ; L = H, C1-C4-alkyl or Ph; and R2 = C1-C4-alkyl, Ph or a polyalkyleneoxide homopolymer or water sol. polyalkyleneoxide contg. copolymer, having a mol. wt. of from about 1,000 to about 20,000. I are prepd. by reacting taxol first with carbonyl diimidazole, bis-succinimidyl carbonate, phosgene or p-nitrophenyl chloroformate, followed by acetic hydrazide, t-Bu carbazate, polyethylene glycol hydrazide or carbazate. I are useful in the treatment of neoplastic disease, tumor burden, metastasis of neoplasms and recurrences of tumor and neoplastic growths.

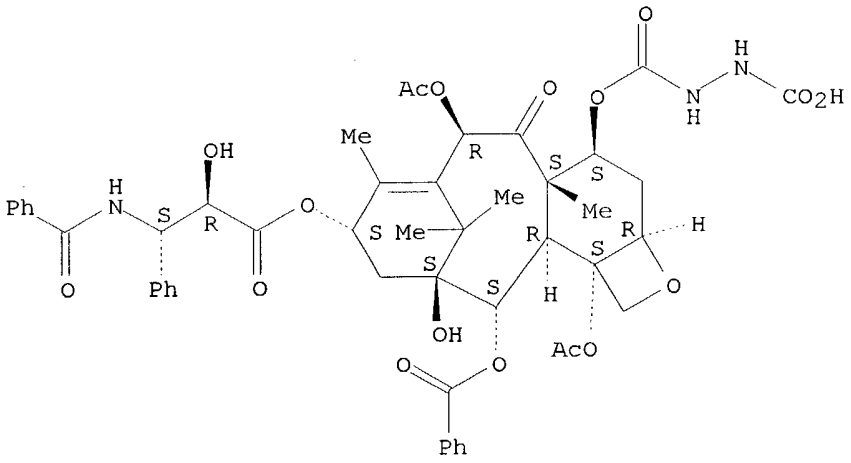
IT **180965-73-5DP**, 7-(Carboxyhydrazidocarbonyl)taxol, polyethylene glycol deriv. ester **180965-75-7P 180965-76-8P**, 7-(Acetohydrazidocarbonyl)taxol
RL: BAC (Biological activity or effector, except adverse); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(taxol 7-carbazates with improved water-soly. and/or enhanced therapeutic activity)

RN 180965-73-5 CAPLUS

CN 1,2-Hydrazinedicarboxylic acid, mono[6,12b-bis(acetyloxy)-9-[3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]

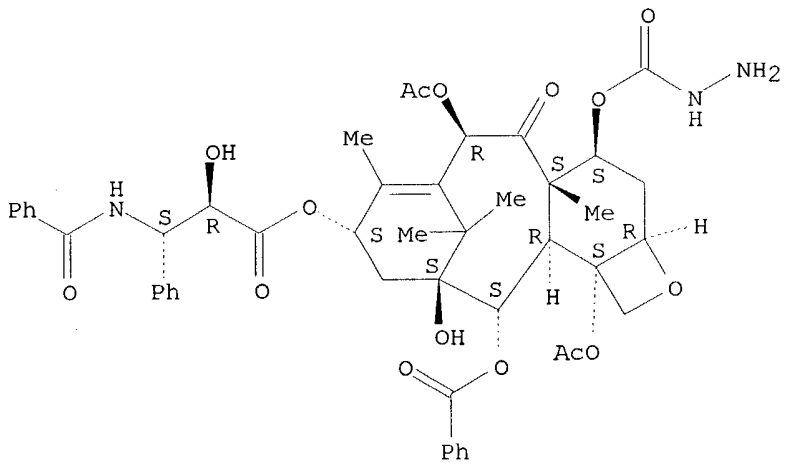
ester,
[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(2R*,[redacted]),11.alpha
.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



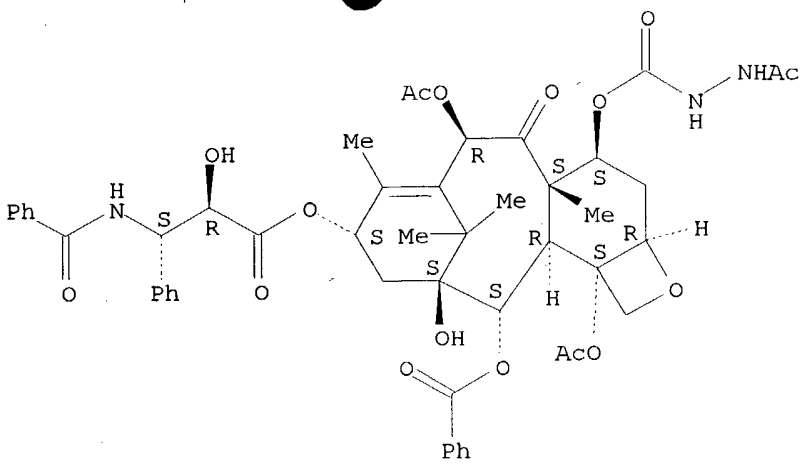
RN 180965-75-7 CAPLUS
CN Hydrazinecarboxylic acid, 6,12b-bis(acetyloxy)-9-[3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl ester,
[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(2R*,3S*),11.alpha
.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 180965-76-8 CAPLUS
CN Hydrazinecarboxylic acid, 2-acetyl-, 6,12b-bis(acetyloxy)-9-[3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl ester,
[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(2R*,3S*),11.alpha
.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



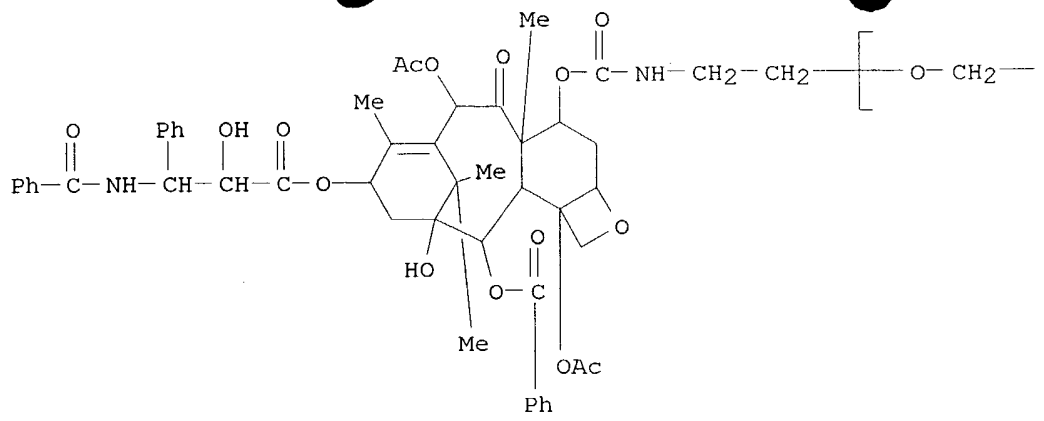
L3 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:434116 CAPLUS
DOCUMENT NUMBER: 125:150894
TITLE: PEG modified anticancer drugs: synthesis and biological activity
AUTHOR(S): Pendri, Annapurna; Gilbert, Carl W.; Soundararajan, Soundara; Bolikal, Durgadas; Shorr, Robert G. L.; Greenwald, Richard B.
CORPORATE SOURCE: Enzon Inc., Piscataway, NJ, 08854, USA
SOURCE: J. Bioact. Compat. Polym. (1996), 11(2), 122-134
CODEN: JBCPEV; ISSN: 0883-9115
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Three well known anticancer drugs, doxorubicin, methotrexate and paclitaxel (taxol), have been modified by the permanent attachment of poly(ethylene glycol)(PEG) and evaluated for in vitro cytotoxic activity against murine leukemias P388 and L1210. The relative potencies of the PEG derivs. suggest that modification of antitumor agents with this type of polymer yields compds. that are highly water sol. but less cytotoxic.

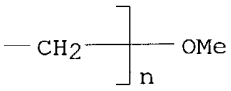
IT **161742-50-3**
RL: RCT (Reactant)
(soly. and cytotoxicity of PEG-modified anticancer doxorubicin, methotrexate and paclitaxel)

RN 161742-50-3 CAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-[2-[[[[6,12b-bis(acetyloxy)-9-[3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]amino]ethyl]-.omega.-methoxy-, [2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(2R*,3S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L3 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:308979 CAPLUS
DOCUMENT NUMBER: 122:214287
TITLE: Highly Water Soluble Taxol Derivatives: 7-Polyethylene Glycol Carbamates and Carbonates
AUTHOR(S): Greenwald, Richard B.; Pendri, Annapurna; Bolikal, Durgadas
CORPORATE SOURCE: Enzon Inc, Piscataway, NJ, 08854, USA
SOURCE: J. Org. Chem. (1995), 60(2), 331-6
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 122:214287

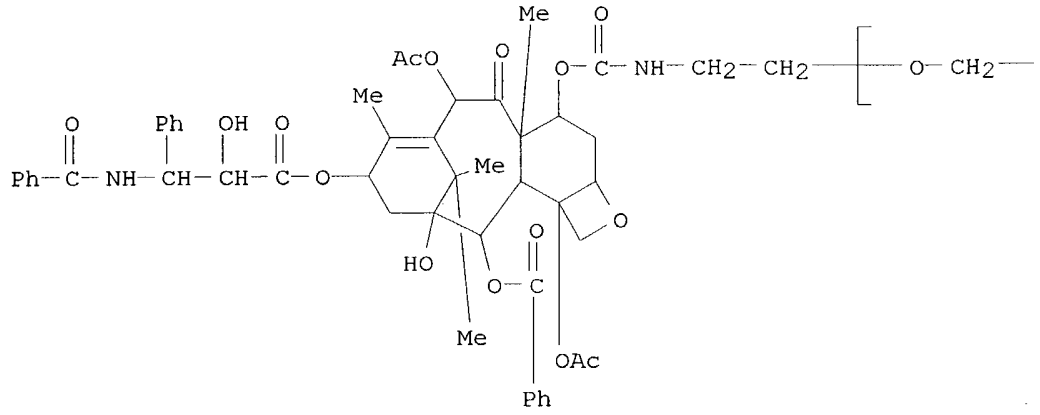
AB The first examples of highly water sol. taxol derivs. (0.1 mmol/mL) were prepd. by the attachment of polyethylene glycol (mol. wt. 2-5 kD) at the 7-position of taxol via a urethane or carbonate linkage. When lower mol. wt. polyethylene glycols (350 and 750) were used, the solubilities were considerably lower (1.87 .times. 10-3 mmol/mL) but still substantially greater than taxol itself. Addnl. 7-substituted taxol derivs. were also prepd. by utilizing small mols. consisting of sugars and ionic and multifunctional compds. However, most of these derivs. had solubilities, calcd. from HPLC retention times, that did not differ significantly from taxol itself. The use of methoxyacetate as a protecting group during these syntheses is discussed.

IT **161742-50-3P 161742-57-0P 161742-58-1P**
161742-59-2P 161742-60-5P 161742-61-6P
161742-62-7P 161742-63-8P 161742-64-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(highly water sol. taxol 7-polyethylene glycol carbamates and carbonates)

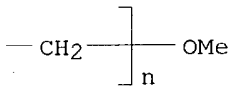
RN 161742-50-3 CAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-[2-[[[[6,12b-bis(acetyloxy)-9-[3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]amino]ethyl]-.omega.-methoxy-, [2aR-

[2a.alpha.,4.beta.,4a[redacted]eta.,6.beta.,9.alpha.(2R*,3S*),[redacted]alpha.,12.alpha.,
12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

PAGE 1-A



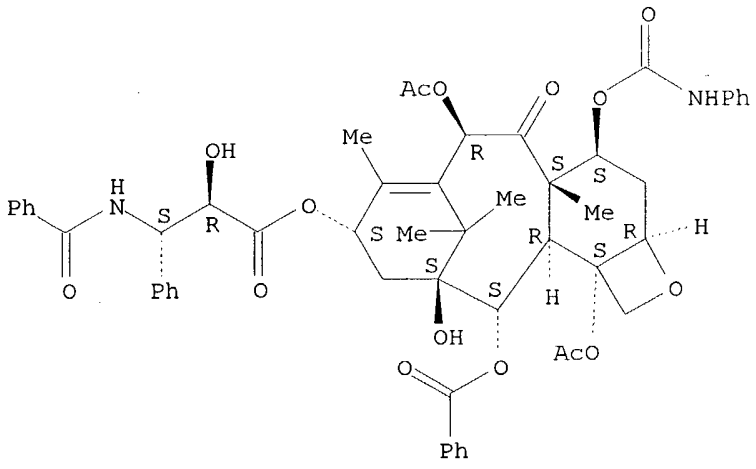
PAGE 1-B



RN 161742-57-0 CAPLUS
CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,
6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-
dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-

[[(phenylamino)carbonyl]oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-
9-yl ester,
[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.b
eta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX
NAME)

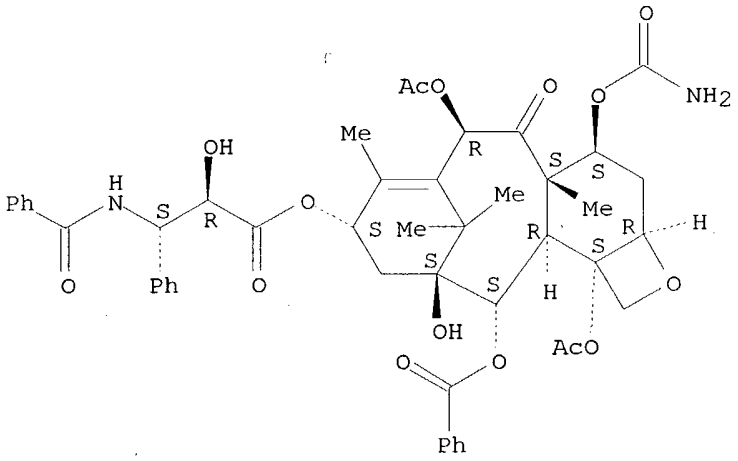
Absolute stereochemistry.



RN 161742-58-1 CAPLUS

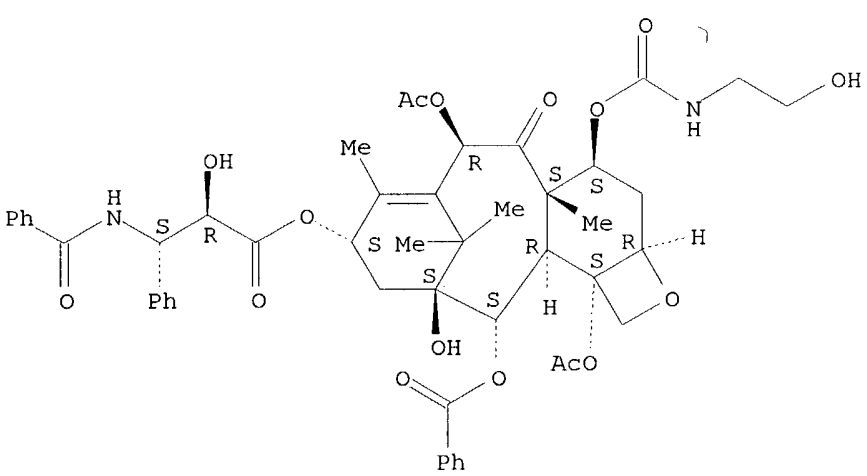
CN Benzenepropanoic [redacted]id, .beta.-(benzoylamino)-.alp[redacted]-hydroxy-, 6,12b-bis(acetyl[redacted])-4-[(aminocarbonyl)oxy]-12-(b[redacted]oyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester,
[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 161742-59-2 CAPLUS
CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4-[[[(2-hydroxyethyl)amino]carbonyl]oxy]-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester,
[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



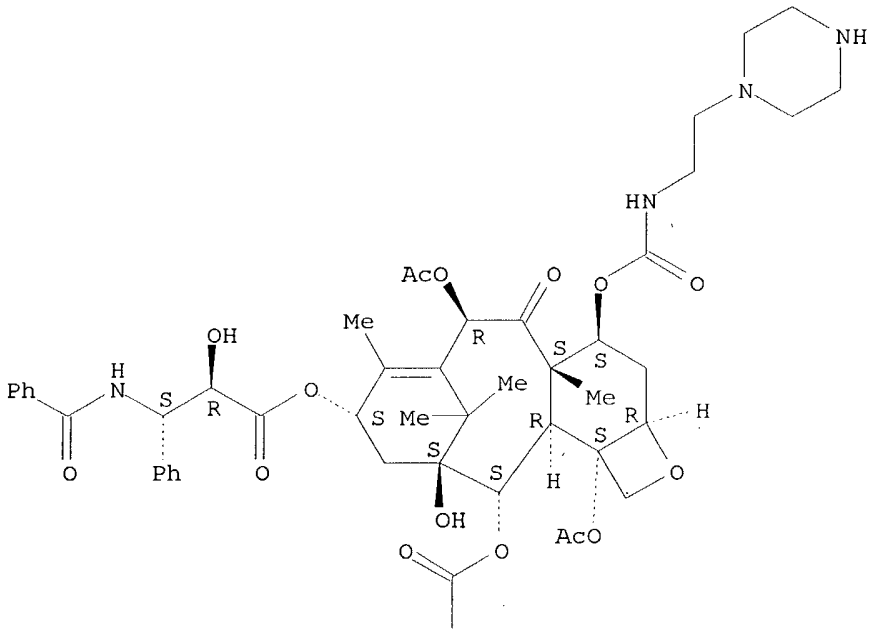
RN 161742-60-5 CAPLUS
CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[[[[2-(1-piperazinyl)ethyl]amino]carbonyl]oxy]-7,11-methano-1H-

cyclodeca[3,4]ben[redacted],2-b]oxet-9-yl ester, [2aR-

[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.
,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

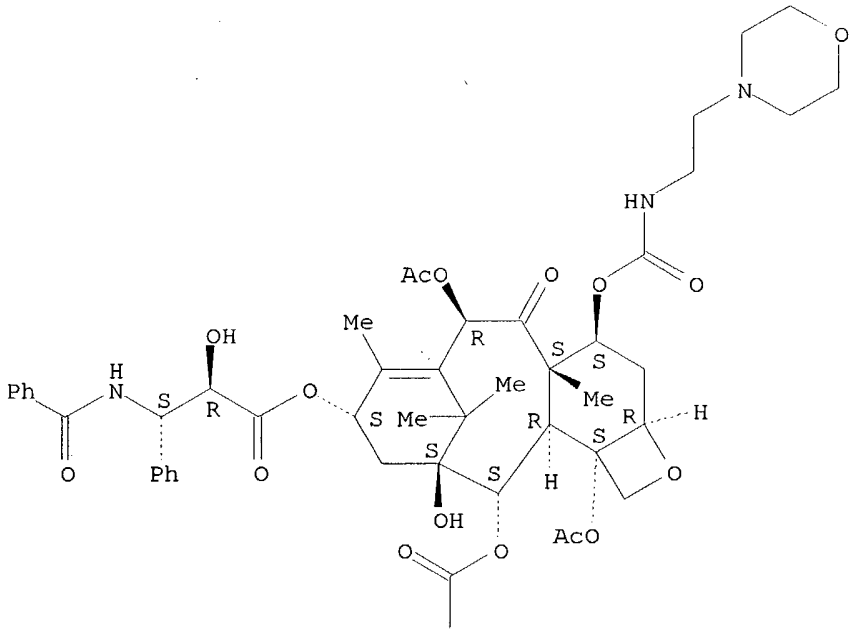
RN 161742-61-6 CAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-4-[[[[2-(4-morpholinyl)ethyl]amino]carbonyl]oxy]-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-

[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.
,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

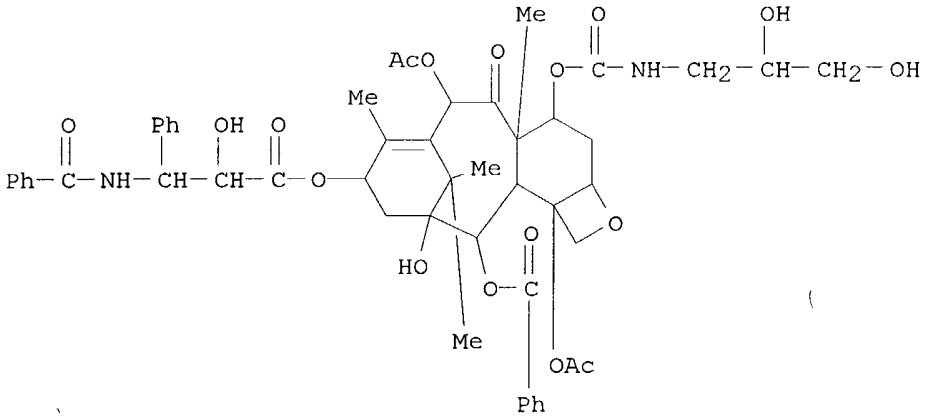
Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

RN 161742-62-7 CAPLUS
CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-4-[[[(2,3-dihydroxypropyl)amino]carbonyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester (9CI) (CA INDEX NAME)



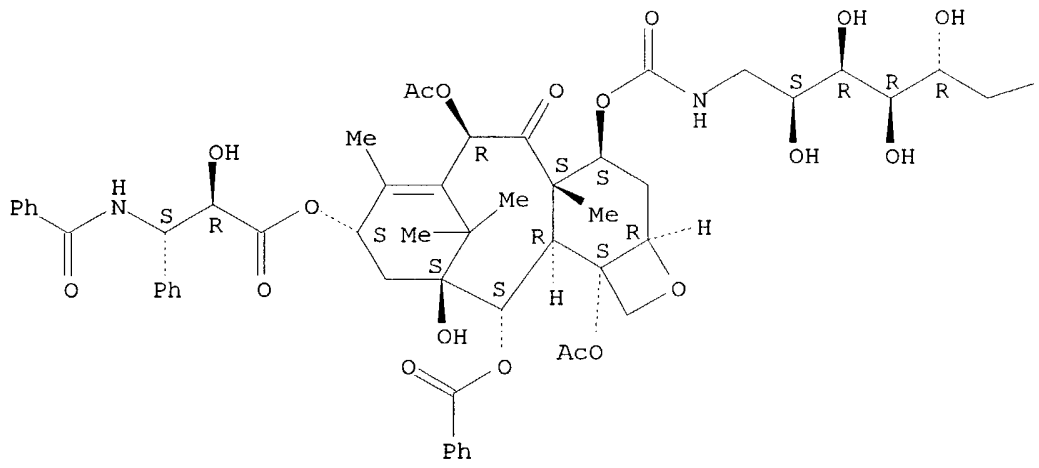
RN 161742-63-8 CAPLUS
CN D-Glucitol, 1-[[[[6,12b-bis(acetyloxy)-9-[3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-

cyclodeca[3,4]ben[redacted],2-b]oxet-4-yl]oxy]carbonyl]am[redacted]-1-deoxy-,

[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(2R*,3S*),11.alpha.,12.al
pha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



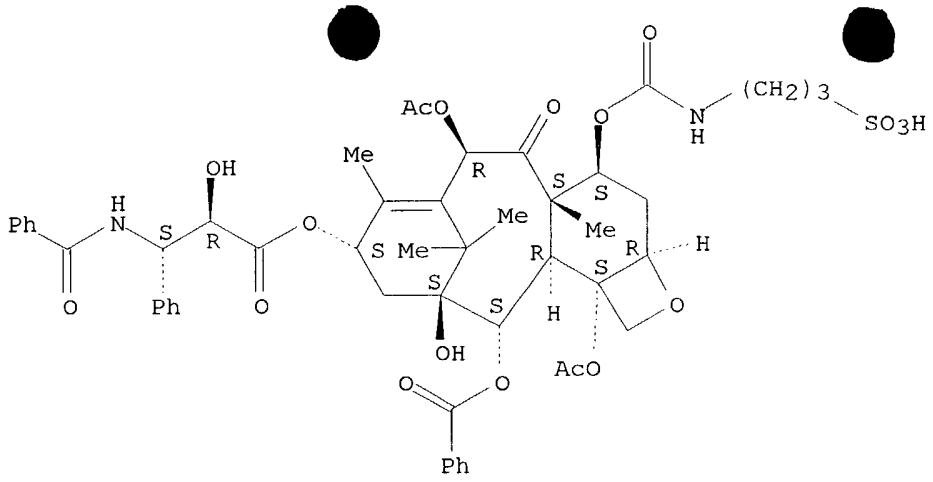
PAGE 1-B

—OH

RN 161742-64-9 CAPLUS
CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,
6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-
dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[[[(3-
sulfopropyl)amino]carbonyl]oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-
b]oxet-9-yl ester, monosodium salt,
[2aR-[2a.alpha.,4.beta.,4a.beta.,6.bet

a.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]
]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● Na

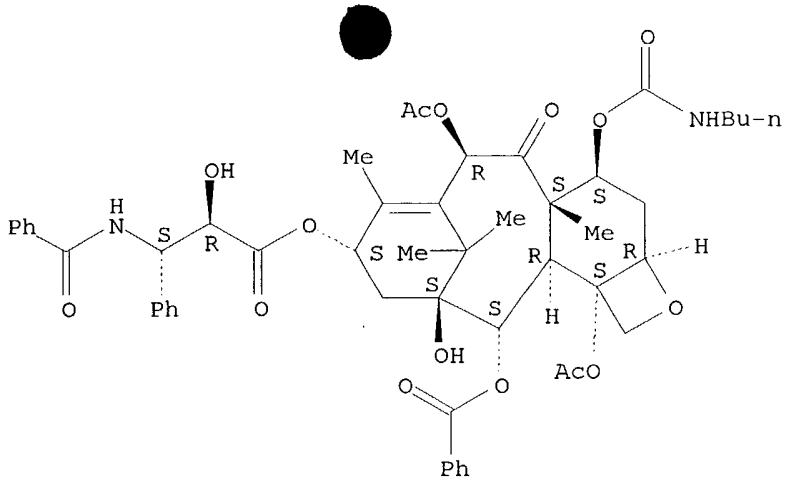
L3 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:139666 CAPLUS
DOCUMENT NUMBER: 122:240034
TITLE: Taxol structure-activity relationships: synthesis and biological evaluation of taxol analogs modified at C-7
AUTHOR(S): Chen, Shu-Hui; Kant, Joydeep; Mamber, Stephen W.; Roth, Gregory P.; Wei, Jian-Mei; Marshall, Dan; Vyas, Dolatrai M.; Farina, Vittorio
CORPORATE SOURCE: Bristol-Myers Squibb Pharm. Res. Inst., Wallingford, CT, 06492-7660, USA
SOURCE: Bioorg. Med. Chem. Lett. (1994), 4(18), 2223-8
CODEN: BMCLE8; ISSN: 0960-894X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of taxol derivs., modified at C-7, is described. This includes sulfonate, silyl ether, ester, carbonate, carbamate, fluoro, dehydro and deoxy derivs. Biol. evaluation shows that these modifications do not usually significantly compromise activity. However, none of the C-7 analogs prepd. thus far have been shown to be better than taxol in both in vitro and in vivo assays.

IT **162081-16-5P 162081-19-8P 162081-21-2P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and cytotoxicity of taxol analogs modified at C-7)

RN 162081-16-5 CAPLUS
CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-4-[[(butylamino)carbonyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

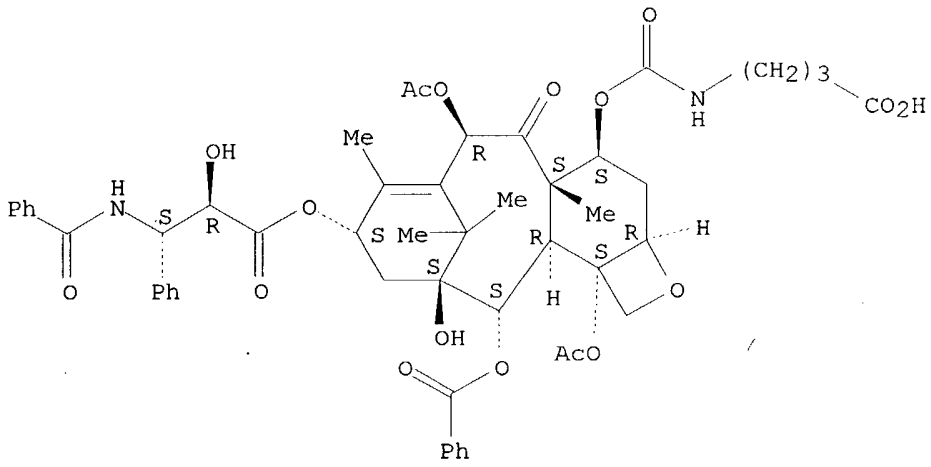
Absolute stereochemistry.



RN 162081-19-8 CAPLUS
CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,

6,12b-bis(acetyloxy)-12-(benzoyloxy)-4-[[[(3-carboxypropyl)amino]carbonyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester,
[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

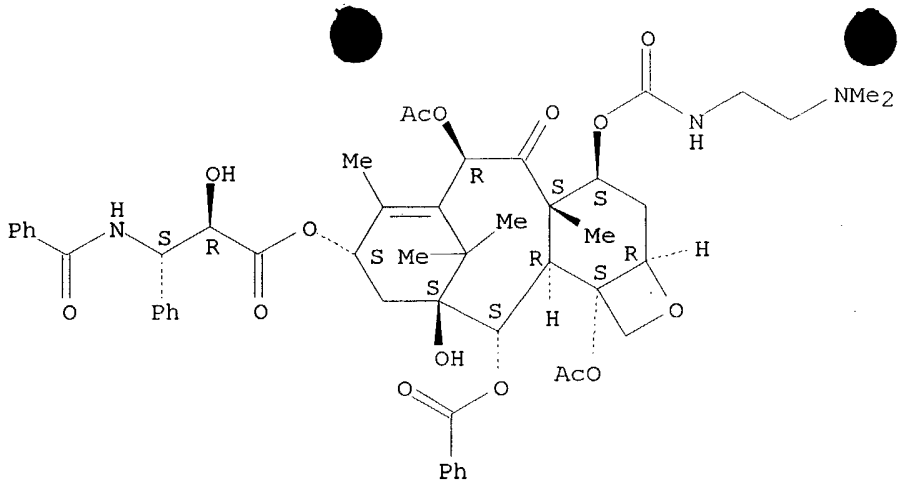
Absolute stereochemistry.



RN 162081-21-2 CAPLUS
CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,

6,12b-bis(acetyloxy)-12-(benzoyloxy)-4-[[[[2-(dimethylamino)ethyl]amino]carbonyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester,
[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:686601 CAPLUS
DOCUMENT NUMBER: 121:286601
TITLE: Taxol-based compositions with enhanced bioactivity
INVENTOR(S): Greenwald, Richard B.; Shorr, Robert G. L.
PATENT ASSIGNEE(S): Enzon, Inc., USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9420089	A1	19940915	WO 1994-US2441	19940308
W: AU, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, NZ, PL, PT, RO, RU, SE, SK, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9463612	A1	19940926	AU 1994-63612	19940308

PRIORITY APPLN. INFO.: US 1993-28743 A 19930309
WO 1994-US2441 W 19940308

OTHER SOURCE(S): MARPAT 121:286601

AB Taxol-based compns. are disclosed based on the formation of 7-carbamates. In certain aspects of the invention, the compns. include polyethylene glycol and have prolonged circulating lives in mammals, are highly water sol. and substantially non-antigenic. Methods of prepn. and treatment using the compns. are also disclosed. 2'-Acetyl-7-PEG 5000 carbamate taxol (I) was prepd. and tested against various malignant human cell lines and against doxorubicin-sensitive and -resistant mouse lymphoid neoplasms. I was >600 times more sol. in water than the unmodified taxol.

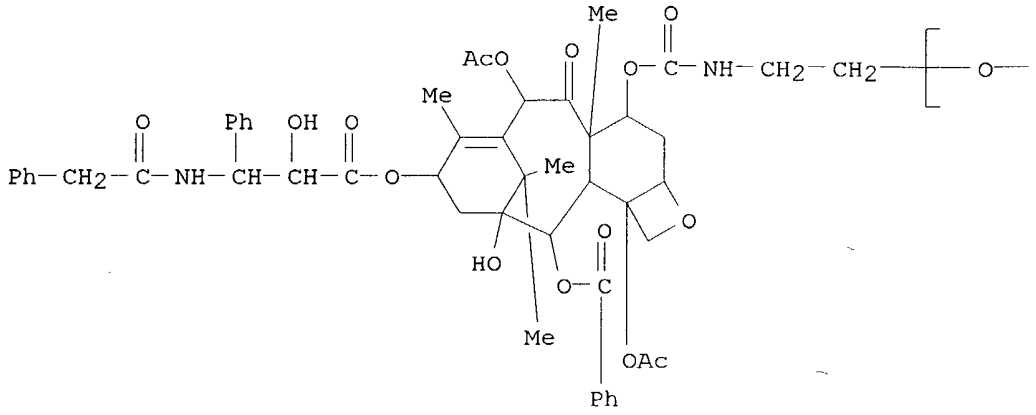
IT **159022-69-2**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(taxol-based compds. with enhanced bioactivity and their prepn.)

RN 159022-69-2 CAPLUS

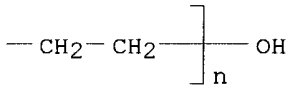
CN Poly(oxy-1,2-ethanediyl), .alpha.-[2-[[[[6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-9-[2-hydroxy-1-oxo-3-phenyl-3-[(phenylacetyl)amino]propoxy]-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]amino]ethyl]-.omega.-hydroxy-, [2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(2R*,3S*),11.alpha.,12.alpha.,

12a.alpha.,12b.a[illegible].]]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



IT **159022-68-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(taxol-based compds. with enhanced bioactivity and their prepn.)
RN 159022-68-1 CAPLUS
CN Glycine, N-[[[6,12b-bis(acetyloxy)-12-(benzoyloxy)-

2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-9-[2-hydroxy-1-oxo-

3-phenyl-3-[(phenylacetyl)amino]propoxy]-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]-,

[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(2R*,3S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)